	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L2	2608	plant adj protein	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/08 13:22			0
2	BRS	L3	4344	soy adj protein	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/08 13:22			0
3	BRS	L4	5647	polylactide	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/08 13:22			0
4	BRS	L5	2	(2 or 3) same 4	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/08 13:24			0
5	BRS	L6	1	5 same composite same extrud$4	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/08 13:25			0
6	BRS	L8	3791	compatibilizer	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/08 13:26			0
7	BRS	L9	68520	oxazoline or polybutadiene	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/08 13:27			0
8	BRS	L10	138	8 same 9	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/08 13:27			0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
9	BRS	L11	31	(2 or 3) same acetylated	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/08 13:28			0
10	BRS	L12	30428	cross-linking adj agent	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/08 13:29			0
11	BRS	L13	33215	cross adj linking adj agent	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/08 13:30			0
12	BRS	L14	254881	(glutaric adj dialdehyde) or epichlorohydrin or formaldehyde or glyoxal or (adipic adj anhydride) or (acetic adj anhydride) or (zinc adj sulfate) or (calcium adj chloride)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/08 13:32			0
13	BRS	L15	3342	14 SAME (12 or 13)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/08 13:32			0
14	BRS	L16	1	5 SAME 15	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/08 13:33			0
15	BRS	L17	1	10 SAME 5	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/08 13:33			0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
16	BRS	L18	128301	PLASTICIZER	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/08 13:33			0
17	BRS	L19	5082	glycerol same 18	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/08 13:34			0
18	BRS	L20	1	5 same 19	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/08 13:34			0
19	BRS	L21	1	zhang adj jinwen.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/08 13:35			0
20	BRS	L22	1	mungara adj perminus.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/08 13:35			0
21	BRS	L23	9	jane adj jay-lin.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/08 13:35			0
22	BRS	L24	1	23 and 5	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/06/08 13:36			0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L1	1431	plant adj protein	USPAT	2003/07/28 11:48			0
2	BRS	L2	2479	soy adj protein	USPAT	2003/07/28 11:48			0
3	BRS	L3	2732	polylactide	USPAT	2003/07/28 11:49			0
4	BRS	L4	0	(1 or 2) same 3 same extrud$4	USPAT	2003/07/28 11:49			0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L1	2732	polylactide	USPAT	2003/07/28 12:01			0
2	BRS	L2	85	protein adj composite	USPAT	2003/07/28 12:02			0
3	BRS	L3	2136	protein same composite	USPAT	2003/07/28 12:02			0
4	BRS	L4	7	1 same 3	USPAT	2003/07/28 12:02			0
5	BRS	L5	342221	extrud$4	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/28 12:09			0
6	BRS	L6	0	4 same 5	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/07/28 12:09			0

```
FILE 'MEDLINE' ENTERED AT 13:38:45 ON 08 JUN 2003

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FILE 'AGRICOLA' ENTERED AT 13:38:45 ON 08 JUN 2003

=> s plant protein
L1       38209 PLANT PROTEIN

=> s soy plant
L2          51 SOY PLANT

=> s mpolylactide
L3           0 MPOLYLACTIDE

=> s polylactide
L4        5609 POLYLACTIDE

=> s (l1 or l2) (p) l4
L5           1 (L1 OR L2) (P) L4

=> d l5 1 ibib abs

L5   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:         2003:319466  CAPLUS
DOCUMENT NUMBER:          138:322139
TITLE:                    Biodegradable plant protein-lactic acid composites and
                          related methods
INVENTOR(S):              Zhang, Jinwen; Mungara, Perminus; Jane, Jay-Lin
PATENT ASSIGNEE(S):       USA
SOURCE:                   U.S. Pat. Appl. Publ., 21 pp., Cont.-in-part of U.S.
                          Ser. No. 564,005.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.   DATE
     ---------------   ----  --------       ---------------   --------
     US 2003078323      A1   20030424       US 2001-976346    20011012
PRIORITY APPLN. INFO.:                     US 1999-132494P   P  19990504
                                           US 2000-564005    A2 20000503
AB   A non-toxic biodegradable   ***plant***     ***protein***   composite
     comprises: 5 to 90 parts soy protein; and 90 to 5 parts of a
       ***polylactide***   .  The composite also preferably includes a
     compatibilizer, a crosslinking agent, and a plasticizer.  The composites
     of this invention offer the advantages of being water resistant and
     biodegradable.


=> s l5 (p) composite (p) extrud?
L6           0 L5 (P) COMPOSITE (P) EXTRUD?

=> s compatibilizer
L7        7105 COMPATIBILIZER

=> s oxazoline or polybutadiene
L8       46617 OXAZOLINE OR POLYBUTADIENE

=> s l7 (p) l8
L9         230 L7 (P) L8

=> s cross linking agent
```

```
L10       6539 CROSS LINKING AGEN

=> s (glutaric dialdehyde) or (epichlorohydrin)or formaldehyde or glyoxal or (adipic anhydride) OR
L11     331624 (GLUTARIC DIALDEHYDE) OR (EPICHLOROHYDRIN) OR FORMALDEHYDE OR
               GLYOXAL OR (ADIPIC ANHYDRIDE) OR (ACETIC ANHYDRIDE) OR (ZINC
               SULFATE) OR (CALCIUM CHLORIDE)

=> S L10 (P) L11
L12         274 L10 (P) L11

=> S PLASTICIZER
L13       69716 PLASTICIZER

=> S L13 (P) GLYCEROL
L14        2653 L13 (P) GLYCEROL

=> d his

     (FILE 'HOME' ENTERED AT 13:38:23 ON 08 JUN 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     13:38:45 ON 08 JUN 2003
L1         38209 S PLANT PROTEIN
L2            51 S SOY PLANT
L3             0 S MPOLYLACTIDE
L4          5609 S POLYLACTIDE
L5             1 S (L1 OR L2) (P) L4
L6             0 S L5 (P) COMPOSITE (P) EXTRUD?
L7          7105 S COMPATIBILIZER
L8         46617 S OXAZOLINE OR POLYBUTADIENE
L9           230 S L7 (P) L8
L10         6539 S CROSS LINKING AGENT
L11       331624 S (GLUTARIC DIALDEHYDE) OR (EPICHLOROHYDRIN)OR FORMALDEHYDE OR
L12          274 S L10 (P) L11
L13        69716 S PLASTICIZER
L14         2653 S L13 (P) GLYCEROL

=> s l5 (p) (l9 or l12 or l14)
L15           0 L5 (P) (L9 OR L12 OR L14)

=> d his

     (FILE 'HOME' ENTERED AT 13:38:23 ON 08 JUN 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     13:38:45 ON 08 JUN 2003
L1         38209 S PLANT PROTEIN
L2            51 S SOY PLANT
L3             0 S MPOLYLACTIDE
L4          5609 S POLYLACTIDE
L5             1 S (L1 OR L2) (P) L4
L6             0 S L5 (P) COMPOSITE (P) EXTRUD?
L7          7105 S COMPATIBILIZER
L8         46617 S OXAZOLINE OR POLYBUTADIENE
L9           230 S L7 (P) L8
L10         6539 S CROSS LINKING AGENT
L11       331624 S (GLUTARIC DIALDEHYDE) OR (EPICHLOROHYDRIN)OR FORMALDEHYDE OR
L12          274 S L10 (P) L11
L13        69716 S PLASTICIZER
L14         2653 S L13 (P) GLYCEROL
L15            0 S L5 (P) (L9 OR L12 OR L14)

=> log y
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                62.15      62.36

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)      SINCE FILE      TOTAL
                                                   ENTRY    SESSION
CA SUBSCRIBER PRICE                                -0.65      -0.65

STN INTERNATIONAL LOGOFF AT 13:45:11 ON 08 JUN 2003
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FILE 'AGRICOLA' ENTERED AT 12:12:40 ON 28 JUL 2003

=> s polylactide
L1        5710 POLYLACTIDE

=> s protein composite
L2         156 PROTEIN COMPOSITE

=> s l1 (p) l2
L3           2 L1 (P) L2

=> diplicate remove l3
DIPLICATE IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> duplicate remove l3
PROCESSING COMPLETED FOR L3
L4            2 DUPLICATE REMOVE L3 (0 DUPLICATES REMOVED)

=> d l4 1-2 ibib abs

L4   ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         2003:319466  CAPLUS
DOCUMENT NUMBER:          138:322139
TITLE:                    Biodegradable plant protein-lactic acid composites and
                          related methods
INVENTOR(S):              Zhang, Jinwen; Mungara, Perminus; Jane, Jay-Lin
PATENT ASSIGNEE(S):       USA
SOURCE:                   U.S. Pat. Appl. Publ., 21 pp., Cont.-in-part of U.S.
                          Ser. No. 564,005.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     US 2003078323      A1   20030424       US 2001-976346   20011012
PRIORITY APPLN. INFO.:                     US 1999-132494P  P  19990504
                                           US 2000-564005   A2 20000503
AB   A non-toxic biodegradable plant   ***protein***     ***composite***
     comprises: 5 to 90 parts soy protein; and 90 to 5 parts of a
       ***polylactide***  . The composite also preferably includes a
     compatibilizer, a crosslinking agent, and a plasticizer.  The composites
     of this invention offer the advantages of being water resistant and
     biodegradable.

L4   ANSWER 2 OF 2  CAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         1991:478840  CAPLUS
DOCUMENT NUMBER:          115:78840
TITLE:                    Ectopic bone induction by partially purified bone
                          extract alone or attached to biomaterials
AUTHOR(S):                Swoboda, H. F.; Wimmer, F. M.; Pfeiffer, K.; Schmidt,
                          K. H.
CORPORATE SOURCE:         Chir. Klin., Univ. Tuebingen, Tuebingen, D-7400,
                          Germany
```

SOURCE: Biomaterials, Artificial Cells, and Artificial Organs (1990), [illegible](3), 383-401
CODEN: BACOEZ; ISSN: 0890-5533
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The formation of new bone is suggested to be caused by interaction of a set of chem. factors with mesenchymal target cells. A specific assembly of factors, i.e. chemotaxis-, adhesion-, proliferation- and differentiation-factors, as well as macromol. structure components, essential for formation of large amts. of ectopic bone was termed osteopoetin. A partially purified osteopoetin contg. bovine bone ext. (OCBE) was used to induce ectopic bone formation. To reduce the amt. of OCBE necessary for bone induction, OCBE was seeded onto different com. available collagens or poly(L-lactic acids). Solid collagens in a sponge-like form were used for the first time to function as an attachment system for an osteoinductive substance. The test substances were implanted into abdominal muscle pouches of male Wistar rats. After 21 days the implants were harvested and evaluated histol. OCBE resulted in the formation of large ossicles contg. hematopoietic bone marrow. The minimal amt. of OCBE to elicit ectopic bone formation can be reduced by a factor of 10 when attached to quickly resorbable collagens, but not when attached to slowly resorbable PL. Collagens are suitable OCBE attachment systems and useful for clin. applications.

=> d his

(FILE 'HOME' ENTERED AT 12:12:15 ON 28 JUL 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 12:12:40 ON 28 JUL 2003
L1 5710 S POLYLACTIDE
L2 156 S PROTEIN COMPOSITE
L3 2 S L1 (P) L2
L4 2 DUPLICATE REMOVE L3 (0 DUPLICATES REMOVED)

=> s protein (p) composite
L5 9918 PROTEIN (P) COMPOSITE

=> s l1 (p) l5
L6 18 L1 (P) L5

=> s l6 (p) extrud?
L7 0 L6 (P) EXTRUD?

=> duplicate remove l6
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L6
L8 11 DUPLICATE REMOVE L6 (7 DUPLICATES REMOVED)

=> d l8 1-11 ibib abs

L8 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:319466 CAPLUS
DOCUMENT NUMBER: 138:322139
TITLE: Biodegradable plant protein-lactic acid composites and related methods
INVENTOR(S): Zhang, Jinwen; Mungara, Perminus; Jane, Jay-Lin
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 21 pp., Cont.-in-part of U.S. Ser. No. 564,005.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003078323	A1	20030424	US 2001-976346	20011012
PRIORITY APPLN. INFO.:			US 1999-132494P P	19990504
			US 2000-564005 A2	20000503

AB A non-toxic biodegradable plant ***protein*** ***composite*** comprises: 5 to 90 parts soy ***protein*** ; and 90 to 5 parts of a ***polylactide*** . The ***composite*** also preferably includes a compatibilizer, a crosslinking agent, and a plasticizer. The

composites of this invention offer the advantages of being water resistant and biodegradable.

L8 ANSWER 2 OF 11 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2003068794 IN-PROCESS
DOCUMENT NUMBER: 22466889 PubMed ID: 12579560
TITLE: Three-dimensional, bioactive, biodegradable, polymer-bioactive glass composite scaffolds with improved mechanical properties support collagen synthesis and mineralization of human osteoblast-like cells in vitro.
AUTHOR: Lu Helen H; El-Amin Saadiq F; Scott Kimberli D; Laurencin Cato T
CORPORATE SOURCE: Center for Advanced Biomaterials and Tissue Engineering, Department of Chemical Engineering, Drexel University, Philadelphia, PA 19104, USA.
SOURCE: JOURNAL OF BIOMEDICAL MATERIALS RESEARCH, (2003 Mar 1) 64A (3) 465-74.
Journal code: 0112726. ISSN: 0021-9304.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20030212
Last Updated on STN: 20030722

AB In the past decade, tissue engineering-based bone grafting has emerged as a viable alternative to biological and synthetic grafts. The biomaterial component is a critical determinant of the ultimate success of the tissue-engineered graft. Because no single existing material possesses all the necessary properties required in an ideal bone graft, our approach has been to develop a three dimensional (3-D), porous ***composite*** of ***polylactide*** -co-glycolide (PLAGA) and 45S5 bioactive glass (BG) that is biodegradable, bioactive, and suitable as a scaffold for bone tissue engineering (PLAGA-BG ***composite***). The objectives of this study were to examine the mechanical properties of a PLAGA-BG matrix, to evaluate the response of human osteoblast-like cells to the PLAGA-BG ***composite*** , and to evaluate the ability of the ***composite*** to form a surface calcium phosphate layer in vitro. Structural and mechanical properties of PLAGA-BG were measured, and the formation of a surface calcium phosphate layer was evaluated by surface analysis methods. The growth and differentiation of human osteoblast-like cells on PLAGA-BG were also examined. A hypothesis was that the combination of PLAGA with BG would result in a biocompatible and bioactive ***composite*** , capable of supporting osteoblast adhesion, growth and differentiation, with mechanical properties superior to PLAGA alone. The addition of bioactive glass granules to the PLAGA matrix resulted in a structure with higher compressive modulus than PLAGA alone. Moreover, the PLAGA-BA ***composite*** was found to be a bioactive material, as it formed surface calcium phosphate deposits in a simulated body fluid (SBF), and in the presence of cells and serum ***proteins*** . The ***composite*** supported osteoblast-like morphology, stained positively for alkaline phosphatase, and supported higher levels of Type I collagen synthesis than tissue culture polystyrene controls. We have successfully developed a degradable, porous, polymer bioactive glass ***composite*** possessing improved mechanical properties and osteointegrative potential compared to degradable polymers of poly(lactic acid-glycolic acid) alone. Future work will focus on the optimization of the ***composite*** scaffold for bone tissue-engineering applications and the evaluation of the 3-D ***composite*** in an in vivo model.

L8 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:32075 CAPLUS
DOCUMENT NUMBER: 137:174811
TITLE: Adsorption and release properties of growth factors from biodegradable implants
AUTHOR(S): Ziegler, J.; Mayr-Wohlfart, U.; Kessler, S.; Breitig, D.; Gunther, K.-P.
CORPORATE SOURCE: Orthopaedic Department (RKU), University of Ulm, Ulm, 89081, Germany
SOURCE: Journal of Biomedical Materials Research (2002), 59(3), 422-428
CODEN: JBMRBG; ISSN: 0021-9304
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The present investigation was performed to study the adsorption behavior of growth factors and their release characteristics from biodegradable

implants in an in vitro study. The authors investigated the stability of growth factors administered on various scaffolds. The authors used porous tricalcium phosphate ceramics (.alpha.-TCP), a neutralized glass ceramics (GB9N), a ***composite*** (***polylactide*** /-glycolide/GB9N), and solvent dehydrated human bone as carriers. Block shaped scaffolds (sized: 7 .times. 7 .times. 10 mm) were loaded with 5 .mu.g of either bone morphogenetic ***protein*** (rxBMP-4), basic fibroblast growth factor (rh-bFGF), or vascular endothelial growth factor (rh-VEGF) solved in 150 .mu.L PBS. The growth factors were labeled with Iodine-125 (I-125) for detecting the adsorbed and released amt. of growth factors by counting the samples for total I-125 activity. The authors obsd. that the adsorption of these growth factors seems to depend on two different parameters: first on the nature of the tested material, and second on the growth factors on their own. The release kinetics of the growth factors from the biodegradable implants can be described as a two phase process-a very rapid release during the first hours by an elution of not adsorbed ***protein*** , followed by a specific release, which depends upon the chem./phys. interaction of the material and the growth factor used. Analyzing the eluted ***proteins*** on SDS-PAGEs rh-VEGF was degraded into a smaller fragment with a size of around 15 kDa, while rxBMP-4 and rh-bFGF showed a complete degrdn. into fragments smaller than 3 kDa after more than 3 days. Although this in vitro study suggests that biodegradable implants might be successfully used as carriers for osteogenic growth factors, the different release kinetics as well as the alteration of their mol. structure including loss of biol. activity should be considered.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:713195 CAPLUS
DOCUMENT NUMBER: 135:262308
TITLE: Polymeric composite materials and their manufacture
INVENTOR(S): Coombes, Allan Gerald Arthur; Downes, Sandra; Griffin, Martin
PATENT ASSIGNEE(S): University of Nottingham, UK; Nottingham Trent University
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001070293	A1	20010927	WO 2001-GB1177	20010319

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2000-6439 A 20000318

AB A method for the prepn. of a polymeric ***composite*** material comprises the steps of (a) forming a porous body of a first polymer; (b) impregnating said porous body with a soln. of a second polymer; and (c) causing or allowing solvent to evap. from said body. The first polymer is preferably a natural polymer, e.g. collagen, and the second polymer is preferably a synthetic polymer, e.g. a polymer selected from the group consisting of poly(.alpha.-hydroxy acid) such as ***polylactide*** , poly(DL-lactide-co-glycolide), poly(.epsilon.-caprolactone), polyorthoesters, polyphosphazenes, hyaluronic acid esters, polyanhydrides, copolymers of such polymers and blends thereof. The ***composites*** are particularly useful in medical and biomedical applications. For example, collagen/polycaprolactone biocomposites were produced by freeze drying 2 mL of 0.25% collagen soln. and impregnation of lyophilized collagen within 2 mL of a polycaprolactone soln. in dichloromethane, followed by solvent evapn. The biocomposite revealed a highly porous morphol. and virtually complete coverage of the collagen component by polycaprolactone. A major fraction (approx. 70-100%) of the collagen content of biocomposites is accessible for digestion by collagenase indicating a high degree of collagen exposure/presentation for interaction with other extracellular matrix ***proteins*** or cells contacting the

biomaterial surface.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:333978 CAPLUS
DOCUMENT NUMBER: 135:185402
TITLE: Poly(lactide-co-glycolide)/hydroxyapatite delivery of BMP-2-producing cells: a regional gene therapy approach to bone regeneration
AUTHOR(S): Laurencin, C. T.; Attawia, M. A.; Lu, L. Q.; Borden, M. D.; Lu, H. H.; Gorum, W. J.; Lieberman, J. R.
CORPORATE SOURCE: Center for Advanced Biomaterials and Tissue Engineering, Department of Chemical Engineering, Drexel University, Philadelphia, PA, 19104, USA
SOURCE: Biomaterials (2001), 22(11), 1271-1277
CODEN: BIMADU; ISSN: 0142-9612
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Currently, functional treatment of fracture non-unions and bone loss remains a significant challenge in the field of orthopaedic surgery. Tissue engineering of bone has emerged as a new treatment alternative in bone repair and regeneration. The authors approach is to combine a polymeric matrix with a cellular vehicle for delivery of bone morphogenetic protein-2 (BMP-2), constructed through retroviral gene transfer. The objective of this study is to develop an osteoinductive, tissue-engineered bone replacement system by culturing BMP-2-producing cells on an osteoconductive, biodegradable, polymeric-ceramic matrix. The hypothesis is that retroviral gene transfer can be used effectively in combination with a biodegradable matrix to promote bone formation. First, the in vitro attachment and growth of transfected BMP-producing cells on a poly(lactide-co-glycolide)/hydroxyapatite (PLAGA-HA) scaffold was examd. Second, the bioactivity of the produced BMP in vitro was evaluated using a mouse model. It was found that the polymer-ceramic scaffold supported BMP-2 prodn., allowing the attachment and growth of retroviral transfected, BMP-2-producing cells. In vivo, the scaffold successfully functioned as a delivery vehicle for bioactive BMP-2, as it induced heterotopic bone formation in a SCID mouse model.
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:599842 CAPLUS
DOCUMENT NUMBER: 136:205375
TITLE: Polymer-bioactive glass composite scaffold for bone tissue engineering: matrix design and in vitro evaluations
AUTHOR(S): Lu, Helen H.; El-Amin, Saadiq A.; Laurencin, Cato T.
CORPORATE SOURCE: Center for Advanced Biomaterials and Tissue Engineering Department of Chemical Engineering, Drexel University, USA
SOURCE: BED (American Society of Mechanical Engineers) (2001), 50(Proceedings of the Bioengineering Conference, 2001), 693-694
CODEN: ASMBEP; ISSN: 1521-4613
PUBLISHER: American Society of Mechanical Engineers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The response of human osteoblast-like cells to the ***polylactide*** , polyglycolide, and their copolymers (PLAGA)-bioactive glass (BG) ***composite*** was studied. The ability of the ***composite*** to form a surface calcium phosphate layer was also examd. The PLAGA-BG ***composites*** were fabricated in both disk and microsphere forms. The three-dimensional (3-D) construct of the ***composite*** was made by heating the microspheres at 70.degree. for 20 h in stainless steel mold. The microsphere-based, 3-D scaffold showed a significant potential as a bone replacement material, and supported the growth, differentiation and mineralization of human osteoblast-like cells. The 3-D construct was bioactive, as it formed surface Ca-P deposits in the presence of cells and serum ***proteins*** . The formation of Ca-P layer may promote its integration with bone tissue.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 11 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2001494269 MEDLINE

DOCUMENT NUMBER: 21202424 Published ID: 11308224
TITLE: Characterization of drug release from diltiazem loaded polylactide microspheres prepared using sodium caseinate and whey protein as emulsifying agents.
AUTHOR: Corrigan O I; Heelan B A
CORPORATE SOURCE: Department of Pharmaceutics, School of Pharmacy, Trinity College, Dublin, Ireland.. ocorrign@tcd.ie
SOURCE: JOURNAL OF MICROENCAPSULATION, (2001 May-Jun) 18 (3) 335-45.
Journal code: 8500513. ISSN: 0265-2048.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010910
Last Updated on STN: 20010910
Entered Medline: 20010906

AB The influence of milk ***protein*** emulsifying agents on the characteristics, particularly drug release, of ***polylactide*** microspheres was investigated. Diltiazem loaded ***polylactide*** (PL) microspheres were successfully prepared using the dairy ***proteins*** , sodium casinate (SC) and whey ***protein*** isolate (WPI) as the emulsifying agents. Microspheres were characerized in terms of microsphere yield, electron microscopy, particle size, drug loading, DSC and XRD analysis and drug release. The yields of microspheres obtained were 53-63% and were independent of the emulsifying agent used. SEM revealed that, regardless of the emulsifying agent employed, the microspheres were of good sphericity, but the surface appearance of the microspheres was not the same in all cases. The milk ***proteins*** resulted in microspheres approximately half the size of those obtained with methylcellulose (MC). Significant differences in drug loading were observed between the three emulgents, the MC systems giving the highest values. Release profiles were sigmoidal in shape and were well fitted to the equation ln (x/1 - x) = k x t - k x tmax, reflecting degradation controlled drug release. The parameter k increased with drug loading, while tmax decreased. The relationships between the release parameters [P(k and tmax)] and loading (L) could be quantified by equations of the form P = a x L(N), N being negative in the case of tmax. Apart from the effect on loading efficiency, neither SC nor WPI appeared to significantly alter drug release. The quantitative relationships observed in this study may have more general application in quantifying drug release from drug-polymer ***composites*** at low loadings where polymer degradation controls drug release.

L8 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:491982 CAPLUS
DOCUMENT NUMBER: 135:285240
TITLE: Study on polylactide as scaffold for bone cell cultivation
AUTHOR(S): Xie, Deming
CORPORATE SOURCE: Institute of Biomedical Engineering, Jinan University, Canton, 510632, Peop. Rep. China
SOURCE: Jinan Daxue Xuebao, Ziran Kexue Yu Yixueban (2000), 21(1), 92-94
CODEN: JDXUET; ISSN: 1000-9965
PUBLISHER: Jinan Daxue Xuebao Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The application of ***polylactide*** as scaffold for cultivating osteoblast was studied. The ***composite*** of bone morphogenetic ***protein*** (BMP) with deacetylated chitosan was prepd. and fixed in ***polylactide*** scaffold. The release of BMP from the ***composite*** was measured. The results showed that BMP-bound ***polylactide*** scaffold may induce the growth of osteoblasts.

L8 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:580808 CAPLUS
DOCUMENT NUMBER: 129:306443
TITLE: Study on the encapsulation of protein in biodegradable polymer microspheres
AUTHOR(S): Li, Xiongwei; Xiao, Jing; Xiong, Chengdong; Deng, Xianmo; Jia, Wenxiang; Meng, Li; Zheng, Zhengxi
CORPORATE SOURCE: Chengdu Inst. Org. Chemistry, Academia Sinica, Chengdu, 610041, Peop. Rep. China
SOURCE: Gaofenzi Cailiao Kexue Yu Gongcheng (1998), 14(4), 93-96

CODEN: G[redacted]GEI; ISSN: 1000-7555
PUBLISHER: "Gaofenz[redacted]ailiao Kexue Yu Gongcheng" Bia[redacted]bu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB Biodegradable ***polylactide*** -b-polyethylene glycol (PLA-PEG) microspheres with micron size carrying human serum albumin (HSA) or outer membrane ***protein*** (OMP) were prepd. out by water-in-oil-in-water ***composite*** emulsion solvent evapn. technique. The data of DSC showed a redn. of the heat of fusion .DELTA.Hp=2.161 J/g of ***protein*** -carrying PLA-PEG microspheres from .DELTA.H0-25.683 J/g of non ***protein*** -carrying PLA-PEG microspheres which indicated that the encapsulation of ***protein*** changed the crystallinity of the PLA-PEG microspheres. The increase of the peaks of endothermic fusion of cryst. of the DSC curve of the ***protein*** -carrying PLA-PEG microspheres identified the effective encapsulation of ***protein*** in microspheres. The quant. anal. of ***protein*** carried out by sampling of abstraction and UV absorbance at 283 nm showed that the content of ***protein*** in PLA-PEG microspheres was related to the nature of ***protein*** and the amt. of ***protein*** in feed. The content of ***protein*** in PLA-PEG microspheres can reach 10%. The adding of surfactant in emulsion improved the encapsulation of ***protein*** in PLA-PEG microspheres.

L8 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1991:478840 CAPLUS
DOCUMENT NUMBER: 115:78840
TITLE: Ectopic bone induction by partially purified bone extract alone or attached to biomaterials
AUTHOR(S): Swoboda, H. F.; Wimmer, F. M.; Pfeiffer, K.; Schmidt, K. H.
CORPORATE SOURCE: Chir. Klin., Univ. Tuebingen, Tuebingen, D-7400, Germany
SOURCE: Biomaterials, Artificial Cells, and Artificial Organs (1990), 18(3), 383-401
CODEN: BACOEZ; ISSN: 0890-5533
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The formation of new bone is suggested to be caused by interaction of a set of chem. factors with mesenchymal target cells. A specific assembly of factors, i.e. chemotaxis-, adhesion-, proliferation- and differentiation-factors, as well as macromol. structure components, essential for formation of large amts. of ectopic bone was termed osteopoetin. A partially purified osteopoetin contg. bovine bone ext. (OCBE) was used to induce ectopic bone formation. To reduce the amt. of OCBE necessary for bone induction, OCBE was seeded onto different com. available collagens or poly(L-lactic acids). Solid collagens in a sponge-like form were used for the first time to function as an attachment system for an osteoinductive substance. The test substances were implanted into abdominal muscle pouches of male Wistar rats. After 21 days the implants were harvested and evaluated histol. OCBE resulted in the formation of large ossicles contg. hematopoietic bone marrow. The minimal amt. of OCBE to elicit ectopic bone formation can be reduced by a factor of 10 when attached to quickly resorbable collagens, but not when attached to slowly resorbable PL. Collagens are suitable OCBE attachment systems and useful for clin. applications.

L8 ANSWER 11 OF 11 MEDLINE on STN
ACCESSION NUMBER: 91274555 MEDLINE
DOCUMENT NUMBER: 91274555 PubMed ID: 2098172
TITLE: Development of synthetic bone-repair materials for craniofacial reconstruction.
AUTHOR: Desilets C P; Marden L J; Patterson A L; Hollinger J O
CORPORATE SOURCE: Walter Reed Army Medical Center, Washington, DC 20307-5300.
SOURCE: JOURNAL OF CRANIOFACIAL SURGERY, (1990 Jul) 1 (3) 150-3.
Journal code: 9010410. ISSN: 1049-2275.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Dental Journals
ENTRY MONTH: 199108
ENTRY DATE: Entered STN: 19910818
Last Updated on STN: 19980206
Entered Medline: 19910801
AB In an effort to minimize problems associated with use of bone grafts and bank bone for craniofacial reconstruction, synthetic biodegradable alternatives are under development at the U.S. Army Institute of Dental Research. The focus is on ***composite*** materials in which either

d,l- ***polylactide*** co[redacted]lycolide or porous tricalcium phosphate function as degradable deliv[redacted] systems for bone-inductive ***proteins*** . Availability of synthetic bone-repair materials would eliminate the need for invasive graft-harvesting procedures, the dangers of pathogen transmission from, and immunogenic reaction to bank bone. In addition, synthetics should be more easily sculpted to restore facial contours. Elimination of the disadvantages of natural bone grafts would result in improved reconstructive care for victims of trauma, disease, and congenital deformity. Military surgeons can especially appreciate the potential of a convenient synthetic bone replacement for use in mass casualty situations where access to, and storage facilities for natural bone will be extremely limited. This review updates current treatments and requirements for synthetic bone-repair materials and describes several experimental materials under evaluation at the U.S. Army Institute of Dental Research.

=> d his

(FILE 'HOME' ENTERED AT 12:12:15 ON 28 JUL 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 12:12:40 ON 28 JUL 2003

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L1          5710 S POLYLACTIDE
L2           156 S PROTEIN COMPOSITE
L3             2 S L1 (P) L2
L4             2 DUPLICATE REMOVE L3 (0 DUPLICATES REMOVED)
L5          9918 S PROTEIN (P) COMPOSITE
L6            18 S L1 (P) L5
L7             0 S L6 (P) EXTRUD?
L8            11 DUPLICATE REMOVE L6 (7 DUPLICATES REMOVED)
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=> log y

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-6.51	-6.51

STN INTERNATIONAL LOGOFF AT 12:16:12 ON 28 JUL 2003

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L1	2745	polylactide	USPAT	2003/08/04 09:48			0
2	BRS	L2	1435	plant adj protein	USPAT	2003/08/04 09:48			0
3	BRS	L3	2485	soy adj protein	USPAT	2003/08/04 09:48			0
4	BRS	L4	2777	zein	USPAT	2003/08/04 09:49			0
5	BRS	L5	158573	extrud$4	USPAT	2003/08/04 09:49			0
6	BRS	L6	35	(2 or 3 or 4) same 1	USPAT	2003/08/04 09:49			0
7	BRS	L7	136547	protrude or (thrust adj out)	USPAT	2003/08/04 09:51			0
8	BRS	L8	0	6 same (5 or 7)	USPAT	2003/08/04 09:51			0